=> s octn1

L1 37 OCTN1

=> s l1 (5a) (transporter#)

L2 27 L1 (5A) (TRANSPORTER#)

=> d l2 1-27 bib ab

L2 ANSWER 1 OF 27 MEDLINE
AN 2002384288 IN-PROCESS
DN 22127705 PubMed ID: 12132663
TI Studies on intestinal absorption of sulpiride (1): carrier-mediated uptake
of sulpiride in the human intestinal cell line Caco-2.
AU Watanabe Kazuhiro; Sawano Tetsuya; Terada Kazuaya; Endo Tetsuya; Sakata
Masakatsu; Sato Juichi
CS Hokkaido College of Pharmacy, Otaru, Japan..
watanabe@hokuyakudai.ac.jp
SO BIOLOGICAL AND PHARMACEUTICAL BULLETIN, (2002 Jul) 25 (7) 885-90.
Journal code: 9311984. ISSN: 0918-6158.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20020723
Last Updated on STN: 20020723
AB We investigated whether the uptake of a specific antipsychotic agent,
sulpiride, in Caco-2 cells is mediated by a carrier-mediated system.
Caco-2 cell monolayers were cultured in plastic culture dishes and uptake
and efflux studies were conducted. The determination of sulpiride was
performed by HPLC. At 37 degrees C, sulpiride uptake in pH 6.0 was twice
as much as in pH 7.4. At 4 degrees C, however, no significant difference
was observed between pH 6.0 and 7.4. The uptake at 4 degrees C was
markedly lower than that obtained at 37 degrees C. The subtraction of the
uptake at 4 degrees C from the uptake at 37 degrees C indicated a
saturable process, and the result of the Eadie-Hofstee plot analysis
indicated that the uptake consists of two or more saturable components.
The uptake was significantly inhibited by uncoupler, protonophore, amino
acid modifying agent and proteinase. Sulpiride efflux was
temperature-dependent and was significantly inhibited by uncoupler and
amino acid modifying agent. These findings indicate that sulpiride uptake
and efflux in Caco-2 cells are carrier-mediated. Furthermore, the uptake
was significantly decreased by some substrates and inhibitors of peptide
transporter , PEPT1, and organic cation ***transporters*** ,
OCTN1 and OCTN2, and was significantly increased by preloading
with them. The uptake was also significantly increased by a typical
substrate of P-glycoprotein. From these findings, we presumed that peptide
transporter PEPT1 and organic cation ***transporters***
OCTN1 and OCTN2 are involved with this uptake. P-glycoprotein may
also contribute to the efflux of sulpiride.

L2 ANSWER 2 OF 27 MEDLINE
AN 2002013690 MEDLINE
DN 21307239 PubMed ID: 11414662
TI Agmatine and putrescine uptake in the human glioma cell line SK-MG-1.
AU Molderings G J; Bonisch H; Gothert M; Bruss M
CS Institut fur Pharmakologie und Toxikologie, U niversitat Bonn, Germany..
molderings@uni-bonn.de
SO NAUNYN-SCHMIEDEBERGS ARCHIVES OF PHARMACOLOGY, (2001 Jun) 363 (6) 671-9.
Journal code: 0326264. ISSN: 0028-1298.
CY Germany: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200112
ED Entered STN: 20020121
Last Updated on STN: 20020121
Entered Medline: 20011204
AB The pharmacological properties of a specific agmatine uptake mechanism
were investigated in the human glioma cell line SK-MG-1 and compared with
those of the putrescine transporter expressed by the same cells and with
those of several other organic cation transport systems or ion channels
reported in the literature. The specific accumulation of [14C]agmatine at
37 degrees C above nonspecific accumulation at 4 degrees C was
energy-dependent and saturable with a Vmax of 64.3+/-3.5 nmol/min per mg
protein and a Km of 8.6+/-1.4 microM. Specific accumulation was attenuated
by replacement of extracellular Na+ by choline by 65%, not affected by
lithium and enhanced by replacement by sucrose. Phentolamine, clonidine,
1,3-di(2-tolyl)guanidine, histamine, putrescine, spermine and spermidine
were inhibitors of specific [14C]agmatine accumulation. In contrast,
corticosterone, desipramine, O-methylisoprenaline, cirazoline, moxonidine,
L-arginine, L-lysine, verapamil, nifedipine and CdCl2 at concentrations up
to 10 mM failed to inhibit specific [14C]agmatine accumulation, thus
excluding that the latter is mediated by amino acid or monoamine carriers,
by Ca2+ channels or by the organic cation ***transporters*** OCT1,
OCT2, OCT3, ***OCTN1*** or OCTN2. The pattern of activity of
inhibitory compounds was also different from that determined for specific
putrescine accumulation found in the same cells (Km 1.3+/-0.1 microM, Vmax
26.1+/-0.4 nmol/min per mg protein) ruling out an identity of the specific
[14C]agmatine and [14C]putrescine accumulation mechanisms. It is concluded
that specific accumulation of agmatine in human glioma cells is

mediated
by a specific transporter whose pharmacological properties are not identical to those of the agmatine transporter previously identified in
rat brain synaptosomes and to other so far known carrier mechanisms for
organic cations and ion channels. The agmatine uptake system may be
important for the regulation of the extracellular concentration of agmatine in man.

L2 ANSWER 3 OF 27 MEDLINE
AN 2001464806 MEDLINE
DN 21400977 PubMed ID: 11509010
TI Carnitine transport by organic cation transporters and systemic carnitine
deficiency.
AU Lahjouji K; Mitchell G A; Qureshi I A
CS Division of Medical Genetics, Hopital Sainte-Justine, 3175 Cote Sainte-Catherine, Montreal, Quebec H3T 1C5, Canada.
SO MOLECULAR GENETICS AND METABOLISM, (2001 Aug) 73 (4) 287-97. Ref: 56
Journal code: 9805456. ISSN: 1096-7192.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200111
ED Entered STN: 20010820
Last Updated on STN: 20011105
Entered Medline: 20011101
AB The intracellular homeostasis is controlled by different membrane
transporters. Organic cation transporters function primarily in the elimination of cationic drugs, endogenous amines, and other xenobiotics in
tissues such as the kidney, intestine, and liver. Among these molecules,
carnitine is an endogenous amine which is an essential cofactor for mitochondrial beta-oxidation. Recently, a new family of transporters,
named OCT (organic cation transporters) has been described. In this
minireview, we present the recent knowledge about OCT and focus on
carnitine transport, more particularly by the OCTN2. The importance of
this sodium-dependent carnitine cotransporter, OCTN2, comes from various
recently reported mutations in the gene which give rise to the primary
systemic carnitine deficiency (SCD; OMIM 212140). The SCD is an autosomal
recessive disorder of fatty acid oxidation characterized by skeletal myopathy, progressive cardiomyopathy, hypoglycemia and hyperammonemia.
Most of the OCTN2 mutations identified in humans with SCD result in loss
of carnitine transport function. Identifying these mutations will allow an
easy targeting of the SCD syndrome. The characteristics of the juvenile
visceral steatosis (jvs) mouse, an animal model of SCD showing similar
symptoms as humans having this genetic disorder, are also described. These
mice have a mutation in the gene encoding the mouse carnitine transporter
octn2. Although various OCTN carnitine transporters have been identified
and functionally characterized, their membrane localization and regulation
are still unknown and must be investigated. This knowledge will also help
in designing new drugs that regulate carnitine transport activity.
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L2 ANSWER 4 OF 27 MEDLINE
AN 2001345562 MEDLINE
DN 21301739 PubMed ID: 11408531
TI Comparison of "type I" and "type II" organic cation transport by organic
cation transporters and organic anion-transporting polypeptides.
AU van Montfoort J E; Muller M; Groothuis G M; Meijer D K; Koepsell H; Meier
P J
CS Department of Pharmacokinetics and Drug Delivery, Groningen University
Institute for Drug Exploration, Groningen, The Netherlands.
SO JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (2001 Jul) 298 (1)
110-5.
Journal code: 0376362. ISSN: 0022-3565.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200107
ED Entered STN: 20010723
Last Updated on STN: 20010723
Entered Medline: 20010719
AB Previous inhibition studies with taurocholate and cardiac glycosides
suggested the presence of separate uptake systems for small "type I"
(system1) and for bulky "type II" (system2) organic cations in rat hepatocytes. To identify the transport systems involved in type I and type
II organic cation uptake, we compared the organic cation transport properties of the rat and human organic cation transporter 1 (rOCT1;
hOCT1) and of the organic anion-transporting polypeptides 2 and A (rat
Oatp2; human OATP-A) in cRNA-injected Xenopus laevis oocytes. Based on
characteristic cis-inhibition patterns of rOCT1-mediated tributylmethylammonium and Oatp2-mediated rocuronium uptake, rOCT1 and
Oatp2 could be identified as the organic cation uptake systems1 and 2,
respectively, in rat liver. While hOCT1 exhibited similar transport properties as rOCT1, OATP-A- but not Oatp2-mediated rocuronium uptake was
inhibited by the OATP-A substrate N-methyl-quinidine. The latter substrate
was also transported by rOCT1 and hOCT1, demonstrating distinct organic
cation transport activities for rOCT1 and Oatp2 and overlapping organic
cation transport activities for hOCT1 and OATP-A. Finally, the data
demonstrate that unmethylated quinidine is transported by rOCT1, hOCT1,
and OATP-A at pH 6.0, but not at pH 7.5, indicating that quinidine
requires a positive charge for carrier-mediated uptake into hepatocytes.
In conclusion, the studies demonstrate that in rat liver the suggested
organic cation uptake systems1 and 2 correspond to rOCT1 and

Oatp2,
respectively. However, the rat-based type I and II organic cation transporter classification cannot be extended without modification from
rat to human.

L2 ANSWER 5 OF 27 MEDLINE
AN 2001131179 MEDLINE
DN 20576747 PubMed ID: 11135053
TI Regulation of renal tubular secretion of organic compounds.
AU Berkhin E B; Humphreys M H
CS Division of Nephrology, San Francisco General Hospital, University of
California San Francisco, San Francisco, California 94143, USA.
SO KIDNEY INTERNATIONAL, (2001 Jan) 59 (1) 17-30. Ref: 169
Journal code: 0323470. ISSN: 0085-2538.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200103
ED Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010301
AB BACKGROUND: Information on the molecular basis underlying organic anion
and cation transport in renal tubules has expanded in recent years with
the identification and characterization of numerous transporters. However,
little is known about the regulation of this transport. METHODS: Both
English and Russian language studies dealing with the regulation of
organic ion transport by the kidney have been reviewed. RESULTS: This
review summarizes the literature on the physiological and pharmacological
aspects of the regulation of organic ion transport, linking this
information where possible to underlying transport mechanisms. Current
models of the tubular secretion of organic anions and cations are
reviewed. Factors that inhibit or enhance tubular secretion of xenobiotics
are described, and their influence on proximal tubule cell transport and
function is discussed. Important roles for substrate stimulation, the
adrenergic nervous system, numerous hormones, P-glycoprotein, and protein
kinase C activity have been identified. CONCLUSIONS: Despite considerable
advances in the understanding of basic transport pathways and mechanisms
involved in the tubular secretion of organic compounds, there is still
relatively little information on the regulation of this transport. Studies
combining the techniques of integrative and cell physiology and molecular
biology will provide significant new insights into the pathways regulating
the tubular transport of these compounds.

L2 ANSWER 6 OF 27 MEDLINE
AN 2001098490 MEDLINE
DN 20568258 PubMed ID: 11010964
TI Molecular and functional characterization of organic cation/carnitine
transporter family in mice.
AU Tamai I; Ohashi R; Nezu J I; Sai Y; Kobayashi D; Oku A; Shimane M; Tsuji A
CS Faculty of Pharmaceutical Sciences, Kanazawa University, Kanazawa
920-0934, Japan.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Dec 22) 275 (51) 40064-72.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-AB016257; GENBANK-AB018436
EM 200102
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010201
AB Carnitine is essential for beta-oxidation of fatty acids, and a defect of
cell membrane transport of carnitine leads to fatal systemic carnitine
deficiency. We have already shown that a defect of the organic
cation/carnitine transporter OCTN2 is a primary cause of systemic
carnitine deficiency. In the present study, we further isolated and
characterized new members of the OCTN family, OCTN1 and -3, in mice. All
three members were expressed commonly in kidney, and OCTN1 and -2 were
also expressed in various tissues, whereas OCTN3 was characterized by
predominant expression in testis. When their cDNAs were transfected into
HEK293 cells, the cells exhibited transport activity for carnitine and/or
the organic cation tetraethylammonium (TEA). Carnitine transport by OCTN1
and OCTN2 was Na(+)-dependent, whereas that by OCTN3 was
Na(+)-independent. TEA was transported by OCTN1 and OCTN2 but not by
OCTN3. The relative uptake activity ratios of carnitine to TEA were 1.78,
11.3, and 746 for OCTN1, -2, and -3, respectively, suggesting high
specificity of OCTN3 for carnitine and significantly lower carnitine
transport activity of OCTN1. Thus, OCTN3 is unique in its limited tissue
distribution and Na(+)-independent carnitine transport, whereas OCTN1
efficiently transported TEA with minimal expression of carnitine transport
activity and may have a different role from other members of the OCTN
family.

L2 ANSWER 7 OF 27 MEDLINE
AN 2000383805 MEDLINE
DN 20286310 PubMed ID: 10825452
TI Structural and functional characteristics and tissue distribution pattern
of rat ***OCTN1*** , an organic cation ***transporter*** , cloned
from placenta.
AU Wu X; George R L; Huang W; Wang H; Conway S J; Leibach F H; Ganapathy V
CS Department of Biochemistry and Molecular Biology, Medical College of
Georgia, Augusta 30912, USA.
NC HL64196 (NHLBI)

SO BIOCHIMICA ET BIOPHYSICA ACTA, (2000 Jun 1) 1466 (1-2) 315-27.
Journal code: 0217513. ISSN: 0006-3002.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200008
ED Entered STN: 20000818
Last Updated on STN: 20000818
Entered Medline: 20000810
AB This report describes the structure, function, and tissue distribution
pattern of rat ***OCTN1*** (novel organic cation ***transporter***
1). The rat ***OCTN1*** cDNA was isolated from a rat placental cDNA
library. The cDNA is 2258 bp long and codes for a protein of 553 amino
acids. Its amino acid sequence bears high homology to human OCTN1 (85%
identity) and rat OCTN2 (74% identity). When expressed heterologously in
mammalian cells, rat OCTN1 mediates Na(+)-independent and pH-dependent
transport of the prototypical organic cation tetraethylammonium. The
transporter interacts with a variety of structurally diverse organic
cations such as desipramine, dimethylamiloride, cimetidine, procainamide,
and verapamil. Carnitine, a zwitterion, interacts with rat OCTN1 with a
very low affinity. However, the transport of carnitine via rat OCTN1 is
not evident in the presence or absence of Na(+). We conclude that rat
OCTN1 is a multispecific organic cation ***transporter*** .
OCTN1 -specific mRNA transcripts are present in a wide variety of
tissues in the rat, principally in the liver, intestine, kidney, brain,
heart and placenta. In situ hybridization shows the distribution pattern
of the transcripts in the brain (cerebellum, hippocampus and cortex),
kidney (cortex and medulla with relatively more abundance in the
cortical-medullary junction), heart (myocardium and valves) and placenta
(labyrinthine zone).

L2 ANSWER 8 OF 27 MEDLINE
AN 2000296966 MEDLINE
DN 20296966 PubMed ID: 10836973
TI Structure of renal organic anion and cation transporters.
AU Burckhardt G; Wolff N A
CS Zentrum Physiologie und Pathophysiologie, Gottingen, Germany..
gburckhardt@veg-physiol.med.uni-goettingen.de
SO AMERICAN JOURNAL OF PHYSIOLOGY. RENAL PHYSIOLOGY, (2000 Jun) 278 (6)
F853-66. Ref: 80
Journal code: 100901990. ISSN: 0363-6127.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200007
ED Entered STN: 20000728
Last Updated on STN: 20000728
Entered Medline: 20000719
AB Here we review the structural and functional properties of organic anion
transporters (OAT1, OAT2, OAT3) and organic cation ***transporters***
(***OCTN1*** , OCTN2, OCT1, OCT2, OCT3), some of which are involved in
renal proximal tubular organic anion and cation secretion. These
transporters share a predicted 12-transmembrane domain (TMD) structure
with a large extracellular loop between TMD1 and TMD2, carrying potential
N-glycosylation sites. Conserved amino acid motifs revealed a relationship
to the sugar transporter family within the major facilitator superfamily.
Following heterologous expression, most OATs transported the model anion
p-aminohippurate (PAH). OAT1, but not OAT2, exhibited PAH-alpha-
ketoglutarate exchange. OCT1-3 transported the model cations
tetraethylammonium (TEA), N(1)-methylnicotinamide, and
1-methyl-4-phenylpyridinium. OCTNs exhibited transport of TEA and/or
preferably the zwitterionic carnitine. Substrate substitution as well as
cis-inhibition experiments demonstrated polyspecificity of the OATs, OCTs,
and OCTN1. On the basis of comparison of the structurally closely related
OATs and OCTs, it may be possible to delineate the binding sites for
organic anions and cations in future experiments.

L2 ANSWER 9 OF 27 MEDLINE
AN 2000207387 MEDLINE
DN 20207387 PubMed ID: 10742984
TI Molecular and functional characteristics of cloned human organic cation
transporters.
AU Dresser M J; Zhang L; Giacomini K M
CS Department of Biopharmaceutical Sciences, University of California San
Francisco 94143, USA.
NC GM36780 (NIGMS)
GM57656 (NIGMS)
SO PHARMACEUTICAL BIOTECHNOLOGY, (1999) 12 441-69. Ref: 40
Journal code: 9310302. ISSN: 1078-0467.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 200005
ED Entered STN: 20000606
Last Updated on STN: 20000606
Entered Medline: 20000523

L2 ANSWER 10 OF 27 MEDLINE
AN 1999234222 MEDLINE
DN 99234222 PubMed ID: 10215651
TI Novel membrane ***transporter*** ***OCTN1*** mediates
multispecific, bidirectional, and pH-dependent transport of organic cations.
AU Yabuuchi H; Tamai I; Nezu J; Sakamoto K; Oku A; Shimane M; Sai Y; Tsuji A
CS Faculty of Pharmaceutical Sciences, Kanazawa University, Kanazawa, Japan.

SO JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (1999 May) 289 (2) 768-73.
Journal code: 0376362. ISSN: 0022-3565.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199905
ED Entered STN: 19990601
Last Updated on STN: 19990601
Entered Medline: 19990520
AB In the present study, functional characteristics of organic cation transporter (OCTN)1, which was cloned as the pH-dependent tetraethylammonium (TEA) transporter when expressed in mammalian human embryonic kidney (HEK)293 cells, were further investigated using Xenopus oocytes as well as HEK293 cells as gene expression systems. When OCTN1-derived complementary RNA was injected into Xenopus oocytes, pH-dependent transport of [14C]TEA was observed as the same in HEK293 cells. In contrast, a replacement of sodium ions with potassium ions in the surrounding medium did not cause any change in [14C]TEA uptake in Xenopus oocytes expressed with OCTN1. In addition, when OCTN1 was expressed in HEK293 cells, efflux of TEA from the cells was pH dependent, with an accelerated rate at acidic external medium pH. Accordingly, membrane potential or sodium ions are suggested to have no influence on [14C]TEA transport and the transport activity of OCTN1 is directly affected by pH itself. Furthermore, addition of the unlabeled TEA in external medium enhanced the efflux of preloaded [14C]TEA. These observations suggest that OCTN1 is a pH-dependent and bidirectional TEA ***transporter*** . ***OCTN1*** -mediated [14C]TEA uptake was inhibited by various organic cations such as cimetidine, procainamide, pyrilamine, quinidine, quinine, and verapamil. In addition, uptakes of cationic compounds such as [3H]pyrilamine, [3H]quinidine, and [3H]verapamil and zwitterionic L-[3H]carnitine were increased by expression of OCTN1 in Xenopus oocytes. Accordingly, OCTN1 was functionally demonstrated to be a multispecific and pH-dependent organic cation transporter, which presumably functions as a proton/organic cation antiporter at the renal apical membrane and other tissues.

L2 ANSWER 11 OF 27 MEDLINE
AN 1999144826 MEDLINE
DN 99144826 PubMed ID: 10022228
TI Recent advances in molecular mechanisms of nephrotoxicity.
AU Endou H
CS Department of Pharmacology and Toxicology, Kyorin University School of Medicine, Tokyo, Japan.. endouh@kyorin-u.ac.jp
SO TOXICOLOGY LETTERS, (1998 Dec 28) 102-103 29-33.
Ref: 17
Journal code: 7709027. ISSN: 0378-4274.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199902
ED Entered STN: 19990311
Last Updated on STN: 19990311
Entered Medline: 19990225
AB Numerous drugs and endogenous compounds are efficiently excreted from the renal proximal tubule via two carrier-mediated pathways, that are organic anion and organic cation transport systems. Since most nephrotoxicants are taken up into renal target cells for further actions, these transport systems seem to be an early event for nephrotoxicity. Recent advances in nephrotoxicity are molecular cloning of several transporters related to important toxic compounds in the kidney. An organic cation transporter 1 (OCT1) was cloned in 1994. On the other hand, we recently isolated a complementary DNA that encodes an organic anion transporter 1 (OAT1) as an anion/dicarboxylate exchanger of the basolateral membrane of proximal tubule. Transepithelial secretion of organic anion consists of an influx of anionic substrates into the cell through the basolateral membrane and their efflux to the urine across the apical membrane. OAT1 displays a remarkably wide substrate specificity, including endogenous substrates, a variety of drugs with different structures and natural toxins. We further isolated homologs of OAT series such as liver-specific OAT2 and kidney-, liver- and brain-expressing OAT3. Because the amino acid sequence of OAT1 shows 38% identity to OCT1, a newly defined 'multispecific organic ion transporter superfamily' will provide potential tools to assess mechanisms of many nephrotoxicants including drugs and xenobiotics, and contribute also in understanding more precisely nephrotoxic mechanisms of chemicals.

L2 ANSWER 12 OF 27 MEDLINE
AN 1998352077 MEDLINE
DN 98352077 PubMed ID: 9685390
TI Molecular and functional identification of sodium ion-dependent, high affinity human carnitine transporter OCTN2.
AU Tamai I; Ohashi R; Nezu J; Yabuuchi H; Oku A; Shimane M; Sai Y; Tsuji A
CS Faculty of Pharmaceutical Sciences, Kanazawa University, 13-1 Takara-machi, Kanazawa 920-0934, Japan.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Aug 7) 273 (32) 20378-82.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-AB015050

EM 199809
ED Entered STN: 19980917
Last Updated on STN: 19980917
Entered Medline: 19980910
AB Primary carnitine deficiency, because of a defect of the tissue plasma
membrane carnitine transporters, causes critical symptoms. However, the
transporter has not been molecularly identified. In this study, we
screened a human kidney cDNA library and assembled a cDNA-encoding OCTN2
as a homologue of the organic cation ***transporter*** ***OCTN1***
, and then we examined the function of OCTN2 as a carnitine transporter.
OCTN2-cDNA encodes a polypeptide of 557 amino acids with 75.8% similarity
to OCTN1. Northern blot analysis showed that OCTN2 is strongly expressed
in kidney, skeletal muscle, heart, and placenta in adult humans. When
OCTN2 was expressed in HEK293 cells, uptake of L-[3H]carnitine was
strongly enhanced in a sodium-dependent manner with Km value of 4.34
microM, whereas typical substrates for previously known organic cation
transporters, tetraethylammonium and guanidine, were not good substitutes.
OCTN2-mediated L-[3H]carnitine transport was inhibited by the D-isomer,
acetyl-D,L-carnitine, and gamma-butyrobetaine with high affinity and by
glycinebetaine with lower affinity, whereas choline, beta-hydroxybutyric
acid, gamma-aminobutyric acid, lysine, and taurine were not inhibitory.
Because the observed tissue distribution of OCTN2 is consistent with the
reported distribution of carnitine transport activity and the functional
characteristics of OCTN2 coincide with those reported for plasma membrane
carnitine transport, we conclude that OCTN2 is a physiologically
important, high affinity sodium-carnitine cotransporter in humans.

L2 ANSWER 13 OF 27 MEDLINE
AN 1998289574 MEDLINE
DN 98289574 PubMed ID: 9618255
TI cDNA sequence, transport function, and genomic organization of human
OCTN2, a new member of the organic cation transporter family.
AU Wu X; Prasad P D; Leibach F H; Ganapathy V
CS Department of Biochemistry and Molecular Biology, Medical College of
Georgia, Augusta 30912, USA.
NC DA 10045 (NIDA)
HD 24451 (NICHD)
HD 33347 (NICHD)
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1998 May 29) 246 (3)
589-95.
Journal code: 0372516. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-AF057164
EM 199807
ED Entered STN: 19980716
Last Updated on STN: 19980716
Entered Medline: 19980702
AB We have cloned OCTN2, a new member of the organic cation transporter
family, from a human placental trophoblast cell line. The hOCTN2 cDNA
codes for a protein of 557 amino acids with twelve putative transmembrane
domains. The octn2 gene, located on human chromosome 5q31, consists of ten
exons. The OCTN2-specific transcript, 3.5 kb in size, is expressed widely
in human tissues and in cell lines of human origin. At the level of amino
acid sequence, OCTN2 is more closely related to OCTN1 than to OCT1, OCT2
and OCT3. When expressed heterologously in HeLa cells, OCTN2 mediates the
transport of tetraethylammonium, a prototypical organic cation, in a
pH-dependent manner. Several organic cations, including the neurotoxins
1-methyl-4-phenylpyridinium,
1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine,
and methamphetamine, compete for the OCTN2-mediated transport process.

L2 ANSWER 14 OF 27 MEDLINE
AN 1998086199 MEDLINE
DN 98086199 PubMed ID: 9426230
TI Cloning and characterization of a novel human pH-dependent organic cation
transporter , ***OCTN1*** .
AU Tamai I; Yabuuchi H; Nezu J; Sai Y; Oku A; Shimane M; Tsuji A
CS Faculty of Pharmaceutical Sciences, Kanazawa University, Japan.
SO FEBS LETTERS, (1997 Dec 8) 419 (1) 107-11.
Journal code: 0155157. ISSN: 0014-5793.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-AB007448
EM 199801
ED Entered STN: 19980206
Last Updated on STN: 19980206
Entered Medline: 19980126
AB cDNA for a novel proton/organic cation ***transporter*** ,
OCTN1 , was cloned from human fetal liver and its transport
activity was investigated. OCTN1 encodes a 551-amino acid protein with 11
transmembrane domains and one nucleotide binding site motif. It is
strongly expressed in kidney, trachea, bone marrow and fetal liver and in
several human cancer cell lines, but not in adult liver. When expressed in
HEK293 cells, OCTN1 exhibited saturable and pH-dependent [3H]tetraethyl
ammonium uptake with higher activity at neutral and alkaline pH than at
acidic pH. Furthermore, treatment with metabolic inhibitors reduced the
uptake, which is consistent with the presence of the nucleotide binding
site sequence motif. Although its subcellular localization and detailed
functional characteristics are not clear at present, OCTN1 appears to be a
novel proton antiporter that functions for active secretion of

cationic
compounds across the renal epithelial brush-border membrane. It may play a
role in the renal excretion of xenobiotics and their metabolites.

L2 ANSWER 15 OF 27 CAPLUS COPYRIGHT 2002 ACS
AN 2002:584217 CAPLUS
TI Studies on intestinal absorption of sulpiride (1): Carrier-mediated uptake
of sulpiride in the human intestinal cell line caco-2
AU Watanabe, Kazuhiro; Sawano, Tetsuya; Terada, Kazuaya; Endo, Tetsuya;
Sakata, Masakatsu; Sato, Juichi
CS Hokkaido College of Pharmacy, Hokkaido, 047-0264, Japan
SO Biological & Pharmaceutical Bulletin (2002), 25(7), 885-890
CODEN: BPBLEO; ISSN: 0918-6158
PB Pharmaceutical Society of Japan
DT Journal
LA English
AB We investigated whether the uptake of a specific antipsychotic agent,
sulpiride, in Caco-2 cells is mediated by a carrier-mediated system.
Caco-2 cell monolayers were cultured in plastic culture dishes and uptake
and efflux studies were conducted. The detn. of sulpiride was performed
by HPLC. At 37.degree.C, sulpiride uptake in pH 6.0 was twice as much as
in pH 7.4. At 4.degree.C, however, no significant difference was obsd.
between pH 6.0 and 7.4. The uptake at 4.degree.C was markedly lower than
that obtained at 37.degree.C. The subtraction of the uptake at 4.degree.C
from the uptake at 37.degree.C indicated a saturable process, and the
result of the Eadie-Hofstee plot anal. indicated that the uptake consists
of two or more saturable components. The uptake was significantly
inhibited by uncoupler, protonophore, amino acid modifying agent and
proteinase. Sulpiride efflux was temp.-dependent and was significantly
inhibited by uncoupler and amino acid modifying agent. These findings
indicate that sulpiride uptake and efflux in Caco-2 cells are
carrier-mediated. Furthermore, the uptake was significantly decreased by
some substrates and inhibitors of peptide ***transporter*** , PEPT1,
and org. cation ***transporters*** , ***OCTN1*** and OCTN2, and was
significantly increased by preloading with them. The uptake was also
significantly increased by a typical substrate of P-glycoprotein. From
these findings, we presumed that peptide ***transporter*** PEPT1 and
org. cation ***transporters*** ***OCTN1*** and OCTN2 are involved
with this uptake. P-glycoprotein may also contribute to the efflux of
sulpiride.

L2 ANSWER 16 OF 27 CAPLUS COPYRIGHT 2002 ACS
AN 2002:85231 CAPLUS
DN 136:336415
TI Tissue distribution and renal developmental changes in rat organic cation
transporter mRNA levels
AU Slitt, A. L.; Cherrington, N. J.; Hartley, D. P.; Leazer, T. M.; Klaassen,
C. D.
CS Department of Pharmacology, Toxicology, University of Kansas Medical
Center, Kansas City, KS, USA
SO Drug Metabolism and Disposition (2002), 30(2), 212-219
CODEN: DMDSAI; ISSN: 0090-9556
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB Org. cation transporters (OCTs) are responsible for excretion of cationic
substances into urine. Tissue OCT expression may be important for the
disposition and excretion of xenobiotics. Therefore, OCT1, OCT2, OCT3,
OCTN1, and OCTN2 mRNA levels were measured in adult rat tissues and rat
kidney tissue at various stages of development from day 0 to 45. OCT1
mRNA expression was highest in kidney and spleen, moderate in skin, and
low in the gastrointestinal tract, brain, lung, thymus, muscle, and
prostate. OCT2 mRNA levels were highest in kidney, with low expression in
other tissues, and with renal OCT2 levels being approx. 4 times higher in
males than that in females. In gonadectomized males, OCT2 mRNA levels
were attenuated to female levels, suggesting a role for testosterone in
OCT2 expression. OCT3 was moderately expressed in kidney and was highest
in blood vessel, skin, and thymus. OCTN1 was expressed in most of the
tissues examd., with relatively higher expression in kidney and ileum and
lower levels in thymus. Lastly, OCTN2 was expressed abundantly in kidney
and ileum, moderately in large intestine, dorsal prostate, bladder,
duodenum, and cerebellum, and minimally in thymus, spleen, and cerebral
cortex. Renal OCT1, OCTN1, and OCTN2 mRNA levels increased gradually from
postnatal day 0 through day 45 in both genders. Renal OCT2 levels
remained the same in males and females through day 25 and then
dramatically increased only in male kidney after day 30. In summary, OCT
mRNA was detected primarily in kidney, and the high level of renal OCT
expression may explain why the kidney is a target organ for xenobiotics
with cationic properties.
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 17 OF 27 CAPLUS COPYRIGHT 2002 ACS
AN 2001:335486 CAPLUS
DN 135:251908
TI Agmatine and putrescine uptake in the human glioma cell line SK-MG-1
AU Molderings, G. J.; Bonisch, H.; Gothert, M.; Bruss, M.
CS Institut fur Pharmakologie und Toxikologie, Universitat Bonn, Bonn, 53113,
Germany
SO Naunyn-Schmiedeberg's Archives of Pharmacology (2001),

363(6), 671-679
CODEN: NSAPCC; ISSN: 0028-1298
PB Springer-Verlag
DT Journal
LA English
AB The pharmacol. properties of a specific agmatine uptake mechanism were
investigated in the human glioma cell line SK-MG-1 and compared with those
of the putrescine transporter expressed by the same cells and with those
of several other org. cation transport systems or ion channels reported in
the literature. The specific accumulation of [C]agmatine at 37 above
nonspecific accumulation at 4 was energy-dependent and saturable with a
Vmax of 64.33.5 nmol/min per mg protein and a Km of 8.61.4 mM. Specific
accumulation was attenuated by replacement of extracellular Na by choline
by 65%, not affected by lithium and enhanced by replacement by sucrose.
Phentolamine, clonidine, 1,3-di-(2-tolyl)guanidine, histamine, putrescine,
spermine and spermidine were inhibitors of specific [14C]agmatine
accumulation. In contrast, corticosterone, desipramine,
O-methylisoprenaline, cirazoline, moxonidine, L-arginine, L-lysine,
verapamil, nifedipine and CdCl2 at concns. up to 10 mM failed to inhibit
specific [14C]agmatine accumulation, thus excluding that the latter is
mediated by amino acid or monoamine carriers, by Ca2+ channels or by the
org. cation ***transporters*** OCT1, OCT2, OCT3, ***OCTN1*** or
OCTN2. The pattern of activity of inhibitory compds. was also different
from that detd. for specific putrescine accumulation found in the same
cells (Km 1.3.+-.0.1 mM, Vmax 26.1.+-.0.4 nmol/min per mg protein) ruling
out an identity of the specific [14C]agmatine and [14C]putrescine
accumulation mechanisms. It is concluded that specific accumulation of
agmatine in human glioma cells is mediated by a specific transporter whose
pharmacol. properties are not identical to those of the agmatine
transporter previously identified in rat brain synaptosomes and to other
so far known carrier mechanisms for org. cations and ion channels. The
agmatine uptake system may be important for the regulation of the
extracellular concn. of agmatine in man.
RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 18 OF 27 CAPLUS COPYRIGHT 2002 ACS
AN 2001:15336 CAPLUS
DN 134:233252
TI Molecular and functional characterization of organic cation/carnitine
transporter family in mice
AU Tamai, Ikumi; Ohashi, Rikiya; Nezu, Jun-Ichi; Sai, Yoshimichi; Kobayashi,
Daisuke; Oku, Asuka; Shimane, Miyuki; Tsuji, Akira
CS Faculty of Pharmaceutical Sciences, Kanazawa University, Kanazawa,
920-0934, Japan
SO Journal of Biological Chemistry (2000), 275(51), 40064-40072
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB Carnitine is essential for .beta.-oxidn. of fatty acids, and a defect of
cell membrane transport of carnitine leads to fatal systemic carnitine
deficiency. We have already shown that a defect of the org.
cation/carnitine transporter OCTN2 is a primary cause of systemic
carnitine deficiency. In the present study, we further isolated and
characterized two new members of the OCTN family, OCTN1 and OCTN3, in
mice. All three members were expressed commonly in kidney, and OCTN1 and
-2 were also expressed in various tissues, whereas OCTN3 was characterized
by predominant expression in testis. When their cDNAs were transfected
into HEK293 cells, the cells exhibited transport activity for carnitine
and/or the org. cation tetraethylammonium (TEA). Carnitine transport by
OCTN1 and OCTN2 was Na+-dependent, whereas that by OCTN3 was
Na+-independent. TEA was transported by OCTN1 and OCTN2 but not by OCTN3.
The relative uptake activity ratios of carnitine to TEA were 1.78, 11.3,
and 746 for OCTN1, -2, and -3, resp., suggesting high specificity of OCTN3
for carnitine and significantly lower carnitine transport activity of
OCTN1. Thus, OCTN3 is unique in its limited tissue distribution and
Na+-independent carnitine transport, whereas OCTN1 efficiently transported
TEA with minimal expression of carnitine transport activity and may have a
different role from other members of the OCTN family.
RE.CNT 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 19 OF 27 CAPLUS COPYRIGHT 2002 ACS
AN 2000:468562 CAPLUS
DN 133:174931
TI Structure of renal organic anion and cation transporters
AU Burckhardt, Gerhard; Wolff, Natascha A.
CS Zentrum Physiologie und Pathophysiologie, Gottingen, D-37073, Germany
SO American Journal of Physiology (2000), 278(6, Pt. 2), F853-F866
CODEN: AJPHAP; ISSN: 0002-9513
PB American Physiological Society
DT Journal; General Review
LA English
AB A review with 80 refs. Here we review the structural and functional
properties of org. anion transporters (OAT1, OAT2, OAT3) and org. cation
transporters (***OCTN1*** , OCTN2, OCT1, OCT2, OCT3), some of
which are involved in renal proximal tubular org. anion and cation
secretion. These transporters share a predicted 12-transmembrane domain
(TMD) structure with a large extracellular loop between TMD1 and TMD2,
carrying potential N-glycosylation sites. Conserved amino acid

motifs
revealed a relationship to the sugar transporter family within the major
facilitator superfamily. Following heterologous expression, most OATs
transported the model anion p-aminohippurate (PAH). OAT1, but not OAT2,
exhibited PAH-.alpha.-ketoglutarate exchange. OCT1-3 transported the
model cations tetraethylammonium (TEA), N1-methylnicotinamide, and
1-methyl-4-phenylpyridinium. OCTNs exhibited transport of TEA and/or
preferably the zwitterionic carnitine. Substrate substitution as well as
cis-inhibition expts. demonstrated polyspecificity of the OATs, OCTs, and
OCTN1. On the basis of comparison of the structurally closely related
OATs and OCTs, it may be possible to delineate the binding sites for org.
anions and cations in future expts.
RE.CNT 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 20 OF 27 CAPLUS COPYRIGHT 2002 ACS
AN 2000:345203 CAPLUS
DN 133:146529
TI Structural and functional characteristics and tissue distribution pattern
of rat ***OCTN1*** , an organic cation ***transporter*** , cloned
from placenta
AU Wu, X.; George, R. L.; Huang, W.; Wang, H.; Conway, S. J.; Leibach, F. H.;
Ganapathy, V.
CS Department of Biochemistry and Molecular Biology, Medical College of
Georgia, Augusta, GA, USA
SO Biochimica et Biophysica Acta (2000), 1466(1-2), 315-327
CODEN: BBACAQ; ISSN: 0006-3002
PB Elsevier Science B.V.
DT Journal
LA English
AB This report describes the structure, function, and tissue distribution
pattern of rat ***OCTN1*** (novel org. cation ***transporter***
1). The rat OCTN1 cDNA was isolated from a rat placental cDNA library.
The cDNA is 2258 bp long and codes for a protein of 553 amino acids. Its
amino acid sequence bears high homol. to human OCTN1 (85% identity) and
rat OCTN2 (74% identity). When expressed heterologously in mammalian
cells, rat OCTN1 mediates Na+-independent and pH-dependent transport of
the prototypical org. cation tetraethylammonium. The transporter
interacts with a variety of structurally diverse org. cations such as
desipramine, dimethylamiloride, cimetidine, procainamide, and verapamil.
Carnitine, a zwitterion, interacts with rat OCTN1 with a very low
affinity. However, the transport of carnitine via rat OCTN1 is not
evident in the presence or absence of Na+. We conclude that rat
OCTN1 is a multispecific org. cation ***transporter***
.
OCTN1-specific mRNA transcripts are present in a wide variety of tissues
in the rat, principally in the liver, intestine, kidney, brain, heart and
placenta. In situ hybridization shows the distribution pattern of the
transcripts in the brain (cerebellum, hippocampus and cortex), kidney
(cortex and medulla with relatively more abundance in the
cortical-medullary junction), heart (myocardium and valves) and placenta
(labyrinthine zone).
RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 21 OF 27 CAPLUS COPYRIGHT 2002 ACS
AN 1999:275091 CAPLUS
DN 131:56832
TI Novel membrane ***transporter*** ***OCTN1*** mediates
multispecific, bidirectional, and pH-dependent transport of organic cations
AU Yabuuchi, Hikaru; Tamai, Ikumi; Nezu, Jun-Ichi; Sakamoto, Kazuki; Oku,
Asuka; Shimane, Miyuki; Sai, Yoshimichi; Tsuji, Akira
CS Faculty of Pharmaceutical Sciences, Kanazawa University, Kanazawa, Japan
SO Journal of Pharmacology and Experimental Therapeutics (1999), 289(2),
768-773
CODEN: JPETAB; ISSN: 0022-3565
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB In the present study, functional characteristics of org. cation
transporter (OCTN)1, which was cloned as the pH-dependent
tetraethylammonium (TEA) transporter when expressed in mammalian human
embryonic kidney (HEK)293 cells, were further investigated using Xenopus
oocytes as well as HEK293 cells as gene expression systems. When
OCTN1-derived complementary RNA was injected into Xenopus oocytes,
pH-dependent transport of [14C]TEA was obsd. as the same in HEK293 cells.
In contrast, a replacement of sodium ions with potassium ions in the
surrounding medium did not cause any change in [14C]TEA uptake in Xenopus
oocytes expressed with OCTN1. In addn., when OCTN1 was expressed in
HEK293 cells, efflux of TEA from the cells was pH dependent, with an
accelerated rate at acidic external medium pH. Accordingly, membrane
potential or sodium ions are suggested to have no influence on [14C]TEA
transport and the transport activity of OCTN1 is directly affected by pH
itself. Furthermore, addn. of the unlabeled TEA in external medium
enhanced the efflux of preloaded [14C]TEA. These observations suggest
that OCTN1 is a pH-dependent and bidirectional TEA transporter.
OCTN1-mediated [14C]TEA uptake was inhibited by various org. cations such
as cimetidine, procainamide, pyrilamine, quinidine, quinine, and
verapamil. In addn., uptakes of cationic compds. such as [3H]pyrilamine,
[3H]quinidine, and [3H]verapamil and zwitterionic L-[3H]carnitine were

increased by expression of OCTN1 in Xenopus oocytes. Accordingly, OCTN1
was functionally demonstrated to be a multispecific and pH-dependent org.
cation transporter, which presumably functions as a proton/org. cation
antiporter at the renal apical membrane and other tissues.
RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 22 OF 27 CAPLUS COPYRIGHT 2002 ACS
AN 1999:194258 CAPLUS
DN 130:250142
TI Cloning of cDNA for ***transporter*** genes ***OCTN1*** and OCTN2
from human and mice
IN Nezu, Jun-ichi; Oku, Asuka
PA Chugai Research Institute for Molecular Medicine, Japan
SO PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9913072	A1	19990318	WO 1998-JP4009	19980907
CA 2302534	AA	19990318	CA 1998-2302534	19980907
AU 9889990	A1	19990329	AU 1998-89990	19980907
AU 736619	B2	20010802		
EP 1020518	A1	20000719	EP 1998-941751	19980907

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRAI JP 1997-260972 A 19970908
JP 1998-156660 A 19980520
WO 1998-JP4009 W 19980907
AB The cDNA of novel genes encoding cation ***transporters*** ***OCTN1*** and OCTN2 are isolated by screening a fetal cDNA library of
human or mice by random sequencing. Proteins OCTN1 and OCTN2 of human are
comprised of 551 and 557 amino acids, resp.; proteins OCTN1 and OCTN2 of
mice are comprised of 553 and 557 amino acids, resp.
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 23 OF 27 CAPLUS COPYRIGHT 2002 ACS
AN 1998:541370 CAPLUS
DN 129:256647
TI Molecular and functional identification of sodium ion-dependent, high
affinity human carnitine transporter OCTN2
AU Tamai, Ikumi; Ohashi, Rikiya; Nezu, Jun-Ichi; Yabuuchi, Hikaru; Oku,
Asuka; Shimane, Miyuki; Sai, Yoshimichi; Tsuji, Akira
CS Faculty of Pharmaceutical Sciences, Kanazawa University, Kanazawa,
920-0934, Japan
SO Journal of Biological Chemistry (1998), 273(32), 20378-20382
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB Primary carnitine deficiency, because of a defect of the tissue plasma
membrane carnitine transporters, causes crit. symptoms. However, the
transporter has not been molecularly identified. In this study, the
authors screened a human kidney cDNA library and assembled a cDNA-encoding
OCTN2 as a homolog of the org. cation ***transporter*** ***OCTN1***
, and then the authors examd. the function of OCTN2 as a carnitine
transporter. OCTN2-cDNA encodes a polypeptide of 557 amino acids with
75.8% similarity to OCTN1. Northern blot anal. showed that OCTN2 is
strongly expressed in kidney, skeletal muscle, heart, and placenta in
adult humans. When OCTN2 was expressed in HEK293 cells, uptake of
L-[3H]carnitine was strongly enhanced in a sodium-dependent manner with Km
value of 4.34 .mu.M, whereas typical substrates for previously known org.
cation transporters, tetraethylammonium and guanidine, were not good
substitutes. OCTN2-mediated L-[3H]carnitine transport was inhibited by
the D-isomer, acetyl-D,L-carnitine, and .gamma.-butyrobetaine with high
affinity and by glycinebetaine with lower affinity, whereas choline,
.beta.-hydroxybutyric acid, .gamma.-aminobutyric acid, lysine, and taurine
were not inhibitory. Because the obsd. tissue distribution of OCTN2 is
consistent with the reported distribution of carnitine transport activity
and the functional characteristics of OCTN2 coincide with those reported
for plasma membrane carnitine transport, the authors conclude that OCTN2
is a physiol. important, high affinity sodium-carnitine cotransporter in
humans.

L2 ANSWER 24 OF 27 CAPLUS COPYRIGHT 2002 ACS
AN 1998:481910 CAPLUS
DN 129:273419
TI Cloning and functional characterization of a novel human pH-dependent
organic cation ***transporter*** , ***OCTN1***
AU Tamai, I.; Yabuuchi, H.; Nezu, J.; Sai, Y.; Oku, A.; Shimane, M.; Tsuji,
A.
CS Faculty of Pharmaceutical Sciences, Kanazawa University, Kanazawa,

920-0934, Japan
SO Proceedings of the International Symposium on Controlled Release of
Bioactive Materials (1998), 25th, 514-515
CODEN: PCRMEY; ISSN: 1022-0178
PB Controlled Release Society, Inc.
DT Journal
LA English
AB The cDNA for a novel org. cation ***transporter*** (***OCTN1***)
was cloned from human fetal liver. The functional properties of OCTN1
were examd. by measuring tetra-Et ammonium (TEA) transport by HEK293
cells. Transport of TEA by OCTN1 is sensitive to pH, suggesting that it
may be a proton/org. cation antiporter. ACTN1 exhibited metabolic energy
dependent TEA uptake, which may indicate a partially primary active
transport. Although its subcellular localization and detailed functional
characteristics are not clear at present, OCTN1 may be a renal proton/org.
cation antiporter functioning at the renal epithelial apical membrane.

L2 ANSWER 25 OF 27 CAPLUS COPYRIGHT 2002 ACS
AN 1997:795702 CAPLUS
DN 128:164138
TI Cloning and characterization of a novel human pH-dependent organic cation
transporter , ***OCTN1***
AU Tamai, Ikumi; Yabuuchi, Hikaru; Nezu, Jun-ichi; Sai, Yoshimichi; Oku,
Asuka; Shimane, Miyuki; Tsuji, Akira
CS Takara-machi, Faculty of Pharmaceutical Sciences, Kanazawa University,
Kanazawa 920, 13-1, Japan
SO FEBS Letters (1997), 419(1), 107-111
CODEN: FEBLAL; ISSN: 0014-5793
PB Elsevier Science B.V.
DT Journal
LA English
AB CDNA for a novel proton/org. cation ***transporter*** , ***OCTN1***
, was cloned from human fetal liver and its transport activity was
investigated. OCTN1 encodes a 551-amino acid protein with 11
transmembrane domains and one nucleotide binding site motif. It is
strongly expressed in kidney, trachea, bone marrow and fetal liver and in
several human cancer cell lines, but not in adult liver. When expressed
in HEK293 cells, OCTN1 exhibited saturable and pH-dependent [3H]tetraethyl
ammonium uptake with higher activity at neutral and alk. pH than at acidic
pH. Furthermore, treatment with metabolic inhibitors reduced the uptake,
which is consistent with the presence of the nucleotide binding site
sequence motif. Although its subcellular localization and detailed
functional characteristics are not clear at present, OCTN1 appears to be a
novel proton antiporter that functions for active secretion of cationic
compds. across the renal epithelial brush-border membrane. It may play a
role in the renal excretion of xenobiotics and their metabolites.

L2 ANSWER 26 OF 27 USPATFULL
AN 2002:186078 USPATFULL
TI Compounds for sustained release of orally delivered drugs
IN Gallop, Mark A., Los Altos, CA, UNITED STATES
Cundy, Kenneth C., Redwood City, CA, UNITED STATES
PI US 2002098999 A1 20020725
AI US 2001-972402 A1 20011005 (9)
PRAI US 2000-238758P 20001006 (60)
US 2000-249804P 20001117 (60)
US 2001-297594P 20010611 (60)
US 2001-297654P 20010611 (60)
US 2001-297641P 20010611 (60)
DT Utility
FS APPLICATION
LREP BURNS DOANE SWECKER & MATHIS L L P, POST OFFICE BOX 1404, ALEXANDRIA,
VA, 22313-1404
CLMN Number of Claims: 42
ECL Exemplary Claim: 1
DRWN 17 Drawing Page(s)
LN.CNT 4303
AB Disclosed are methods for providing sustained systemic blood concentrations of orally delivered drugs. Still further, disclosed are
compounds and pharmaceutical compositions that are used in such methods.

L2 ANSWER 27 OF 27 USPATFULL
AN 2002:16850 USPATFULL
TI Human stress array
IN Chenchik, Alex, Palo Alto, CA, UNITED STATES
Lukashev, Matvey E., Newton, MA, UNITED STATES
PI US 2002009730 A1 20020124
AI US 2001-782909 A1 20010213 (9)
RLI Continuation-in-part of Ser. No. US 1999-441920, filed on 17 Nov 1999,
UNKNOWN
DT Utility
FS APPLICATION
LREP Bret E. Field, BOZICEVIC, FIELD & FRANCIS LLP, 200 Middlefield Road,
Suite 200, Menlo Park, CA, 94025
CLMN Number of Claims: 36
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2377
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Human stress arrays and methods for their use are provided. The subject
arrays include a plurality of polynucleotide spots, each of which is
made up of a polynucleotide probe composition of unique polynucleotides
corresponding to a human stress gene. The subject arrays find use in
hybridization assays, particularly in assays for the identification of
differential gene expression of human stress genes.